REMARKS

This document is filed in reply to the Final Office Action dated July 13, 2010. Applicants have amended claim 4 to correct informalities. No new matter is added. Claims 1, 3-5, and 8-41 are pending in the application. Among them, claims 1, 3-5, 8, 30, and 41 are under examination. Reconsideration of this application is respectfully requested in view of the foregoing claim amendments and the following remarks.

Rejections under 35 USC § 102(e)

Claims 1, 3-5, 8, 30, and 41 remain rejected as allegedly being anticipated by U.S. PG-Pub 2004/0171020 by Ulrich *et al.* ("Ulrich") in light of Kolibachuk *et al.* (Journal. of Bacteriology Nov. 1993, vol. 175(22), pages 7007-7312; "Kolibachuk"). See the Office Action, page 3, lines 5-7.

The claims are directed to an extracellular method of regulating quorum sensing in bacteria expressing LuxR or a homologue thereof. The method includes a step of modulating the activation by a signaling molecule of LuxR or its homologue by administering to the bacteria an antibody which specifically binds LuxR or its homologue. The binding of an antibody to LuxR or the homologue prevents the LuxR or homologue from being activated by its signaling molecule.

In their previous reply filed on April 28, 2010, Applicants pointed out that Ulrich was based on, and entirely consistent with, the erroneous belief held in the art at the filing date of the present invention that LuxR and its homologues were intracellular proteins. Specifically, Applicants noted that Ulrich contains no disclosure or suggestion that LuxR might be found on the outer surface of the bacterial membrane, and therefore does not anticipate the claims at issue, which are drawn to an extracellular method of regulating quorum sensing in bacteria.

Yet, in the present Final Office Action, the Examiner maintained her rejection relying on an "inherency" theory. See the Office Action, page 5, second paragraph.

Applicants respectfully traverse, noting that

> Inherency, … , may not be established by probabilities or possibilities.
> …
> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex*

> *parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

MPEP 2112IV. To support her "inherency" theory, the Examiner cited to Kolibachuk. According to the Examiner, Kolibachuk provided evidence showing that LuxR is a membrane-bound protein.

Applicants, however, note that the alleged Kolibachuk evidence was based on experiments where anti-LuxR antibodies were incubated with a preparation having both "the cytoplasmic membranes and the outer membranes" of bacteria. To that end, Kolibachuk explicitly clarified that "We were not successful in attempts to separate the cytoplasmic membranes and the outer membranes." See pages 7310-7311, bridging sentence, emphases added. It was well known in the art that bacteria have two layers of membranes - the cytoplasmic membranes and the outer membranes. It was also well known in the art that the outer membranes face extracellular environment while the cytoplasmic membranes do not. See, e.g., Qin *et al.* EMBO J. 2000, 19:5212-5221, Fig. 9, copy attached as Exhibit A.

With regards to these two layers of membranes and their relationship with LuxR, Kolibachuk merely made a "suggestion that the N-terminal regulatory domain of LuxR is associated with the **cytoplasmic membranes**." See page 7311, column 1, lines 16-20, (emphasis added). It provides **NO** teaching regarding any association of LuxR with the **outer membranes**.

In view of this fact, one skilled in the relevant art would conclude that there was **NO** "basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic [i.e., extracellular presence of LuxR] necessarily flows from the teachings of the applied prior art," i.e., Kolibachuk or Ulrich for that matter. Accordingly, there is no *prima facie* case of inherency.

Even if there were such a case, which Applicants do not concede, it "can be rebutted by evidence showing that the prior art … do[es] not necessarily possess the characteristics of the claimed [method]. *In re Best,* 562 F.2d at 1255, 195 USPQ at 433." See MPEP 2112.01 I.

In this connection, Applicants turn again to Qin *et al.* (Exhibit A) mentioned above. Qin *et al.* describes cell fractionation experiment with TraR, a LuxR homologue. This article provides evidence that TraR is associated with the cytoplasmic membranes, but not the outer membrane. See, e.g., Fig. 9. This evidence clearly shows that "the prior art do[es] not

necessarily possess the characteristics of the claimed [method]" and therefore successfully rebuts a *prima facie* case of inherency, if any.

Thus, Applicants submit that claims 1, 3-5, 8, 30, and 41 are novel over the cited references.

Rejections under 35 USC § 102 (b)

The Examiner further rejected claims 1, 3-5, 8, 30, and 41 as allegedly being anticipated by U.S. PG-Pub 2003/0165932 by Taga *et al.* ("Taga") in light of Kolibachuk. See the Office Action, page 5, last full paragraph.

According to the Examiner, Taga describes "identification of LsrR: a protein responsible for mediating AI-2 regulation of transcription of the lsr operon" and applying an anti-LsrR antibody to bacteria. Judging from the Examiner's languages, it appears to be her position that LsrR is a "homologue [of LuxR]" as recited in independent claim 1 and, therefore, Taga anticipates claim 1 under 35 U.S.C. 102.

However, "for anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly." MPEP706.02V. Here, the Examiner does not provide any basis for showing that LsrR is a homologue of LuxR as recited in independent claim 1. In other words, Taga does not teach at least the "LuxR or a homologue thereof" "aspect of the claimed invention." Kolibachuk does not rectify this defect of Taga. Thus, Taga in light of Kolibachuk does not anticipate claim 1.

Furthermore, Taga is defective in another aspect – like Ulrich discussed above, it does not teach association of LsrR with the outer membranes. In fact, it does not even teach that LsrR is a membrane protein. To the contrary, it teaches that LsrR is an intracellular, cytoplasmic protein. See, e.g., Figure 25. As discussed above, claim 1 is drawn to an extracellular method of regulating quorum sensing in bacteria expressing LuxR or a homologue thereof. Accordingly, to the extent that LsrR is an intracellular, cytoplasmic protein, Taga in light of Kolibachuk does not anticipate claim 1. Claim 1 is therefore patentable over the cited references on this independent, second ground.

For the above reasons, Applicants submit that claim 1 is patentable over Taga in light of Kolibachuk. Claims 3-5, 8, 30, and 41 depend from claim 1. For at least the same reasons, they

are also patentable. Applicants therefore respectfully request that the Examiner withdraw the ground of rejection.

CONCLUSION

In view of the foregoing remarks, Applicants believe that this application is in a condition for allowance and an early notice to this effect is earnestly solicited. If the Examiner does not believe that such action can be taken at this time or if the Examiner feels that a telephone interview is necessary or desirable, Applicants welcome the Examiner to call the undersigned at 609-844-3020.

The USPTO is authorized to charge Deposit Account No. 50-1943 for any charges in connection with this matter.

Respectfully submitted,

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